REMARKS

Claims 10 and 29-44 are pending in this divisional application. Applicants have elected, with traverse, to prosecute the Group IV claims 10, 30, 31, 33, 36, 37 and 39-42 drawn at least to antibodies against Human Reticulocalbinδ (RCNδ) having SEQ ID NO:3. Applicants reserve the right to prosecute the subject matter of non-elected claims in subsequent divisional applications.

Rejoinder

Applicants submit that, upon allowance of any product claim, the methods of claims 29, 32, 34, 35, 38, 43 and 44, drawn to methods of making and using the products of claims 10, 30, 31, 33, 36-37 and 39-42, and which depend therefrom, should be rejoined and examined in accordance with the Commissioner's Notice in the Official Gazette of March 26, 1996, entitled "Guidance on Treatment of Product and Process Claims in Light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)" which sets forth the rules, upon allowance of product claims, for rejoinder of process claims covering the same scope of products.

Claim rejections under 35 U.S.C. § 112, second paragraph

Claims 36 and 39 have been rejected under 35 U.S.C. § 112, second paragraph for alleged indefiniteness as depending from claims directed to non-elected inventions. Applicants submit that, once product claim 10 is allowed, the method claims 35 and 38 from which claims 36 and 39 depend will be rejoined. Since the patentability of method claims 35 and 38 relies on the novelty and patentability of claim 10, and these claims do not expand the scope of the products recited in claim 10, claims 35 and 38 will be allowable upon rejoinder. Once this has been accomplished, claims 36 and 39 will depend from allowable method claims 35 and 38. Accordingly since Applicants are confident that the Examiner will withdraw the 35 U.S.C. § 112, first paragraph and 35 U.S.C. § 102(a) and § 102(b) rejections against claim 10 and allow claim 10 after considering the arguments submitted below, this rejection of claims 36 and 39 will be moot.

Claim rejections under 35 U.S.C. § 112, first paragraph

Claims 10, 30, 31, 33, 36, 37 and 39-42 have been rejected under 35 U.S.C. § 112, first paragraph as allegedly lacking an adequate written description. In particular, the Office Action asserts:

- Claim 10 recites that the antibody will specifically bind to a polypeptide having 90% identity to SEQ ID NO:3, to biologically active fragments of SEQ ID NO:3, and to immunogenic fragments of SEQ ID NO:3...the specification fails to describe active polypeptides having 90% identity to SEQ ID NO:3, that comprise biologically active fragments of SEQ ID NO:3, and comprise immunogenic fragments of SEQ ID NO:3. (Office Action at page 3.)

While not conceding the propriety of the Examiner's position, claim 10 has been amended to remove the variant and fragment language. It is therefore requested that the written description rejection be withdrawn.

Claim rejections under 35 U.S.C. § 102(a)

Claims 10, 30, 31, 33, 36, 37 and 39-42 have been rejected under 35 U.S.C. § 102(a) as allegedly being anticipated by Yabe et al. (July 18, 1997; J. Biol. Chem. 272:18323-18239). The Office Action asserts that:

- Yabe et al....teach calumenin having 98.2% identity to SEQ ID NO:3. (Office Action at page 4.)

- Yabe et al. made antibodies against calumenin, anti-protein-disulfde isomerase antibody. Given that antibodies bind epitopic structures rather than sequences per se, and the identity between RCNδ and calumenin is high, the antibody made by Yabe et al. will also bind polypeptides having SEQ ID NO:3... (Office Action at page 4.)

- the antibodies were in composition (Claim 31, 37, 40). The antibodies were labeled via conjugation with fluorescein isothiocyanate (Claim 33). Claims 41 and 42 are being considered to be anticipated as well because there appears to be no difference in the antibody made by a Fab expression library or and [sic] immunoglobulin expression library. (Office Action at page 4.)

Applicants strongly disagree with the Examiner's position and traverse the rejection.

The MPEP is clear with regard to the requirements for making a rejection under any subsection of 35 U.S.C. § 102:

> for anticipation under 35 U.S.C. 102, ***the reference must teach every aspect of the claimed invention either explicitly or impliedly***. Any feature not directly taught must be inherently present. (*MPEP 706.02* at page 700-21, Rev. 1, Feb. 2003) [Emphasis added.]

The polypeptide sequence taught by Yabe et al. does not ***teach every aspect of the claimed invention either explicitly or impliedly***. The Examiner has admitted that the polypeptide sequence taught by Yabe et al. (calumenin) is 98.2% identical to SEQ ID NO:3 (RCNδ). (Office Action at page 4.) It is, therefore, possible to make an antibody to SEQ ID NO:3 that does not bind calumenin. Such an antibody is recited in claim 10 as "An isolated antibody ***which specifically binds*** to a polypeptide comprising the amino acid sequence of SEQ ID NO:3." By **"specifically binding"** to SEQ ID NO:3, the claimed antibody ***must*** bind to a polypeptide consisting of SEQ ID NO:3. Accordingly, so long as there are differences, even just one amino acid residue, between the amino acid sequence recited in claim 10 and that disclosed in Yabe et al., an antibody can be produced that can specifically bind to the polypeptide recited in claim 10 and not that of calumenin.

Evidence in support of this premise may be found in Abaza et al., J. Protein Chem. (1992) 11:433-444 (Attachment 1). As taught by Abaza et al., a single amino acid substitution outside the antigenic site on a protein effects antibody binding. This provides scientific support of Applicants' assertion that so long as there are differences, even just one amino acid residue, between the amino acid sequence of claim 10 and those of the prior art, an antibody can be produced that can specifically bind to the polypeptide recited in claim 10 and not those of the prior art. Accordingly, given the amino acid differences between SEQ ID NO:3 and calumenin, one of skill in the art could produce an antibody which binds to the polypeptide recited in claim 10 alone and without cross-reactivity to other polypeptides even those which have extensive sequence identity to SEQ ID NO:3.

Once claim 10 (and therefore claims 30, 36 and 39) has been correctly characterized and considered in its proper context, the ancillary issues regarding antibodies in composition (claims 31, 37 and 40), having a label (claim 33), or being produced by either a Fab expression library or an

immunoglobulin expression library (claims 41 and 42) become moot. For at least the above reasons, Applicants respectfully request that this rejection be withdrawn.

Claim rejections under 35 U.S.C. § 102(b)

Claims 10, 30, 31, 33, 36, 37 and 39-42 have been rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Ozawa et al. (1993; J. Biol. Chem. 268:699-705). The Office Action asserts that:

- Ozawa et al. teach reticulocalbin having 89.1% identity to SEQ ID NO:3. (Office Action at page 4.)
- Ozawa et al. made antibodies against reticulocalbin. Given that antibodies bind epitopic structures rather than sequences per se, and the identity between RCNδ and reticulocalbin is high, the antibody made by Ozawa et al. will also bind polypeptides having SEQ ID NO:3... (Office Action at page 4.)
- the antibodies were in composition (Claim 31, 37, 40)...the antibodies were labeled via conjugation with fluorescein isothiocyanate (Claim 33). Claims 41 and 42 are being considered to be anticipated as well because there appears to be no difference in the antibody made by a Fab expression library or and [sic] immunoglobulin expression library. (Office Action at page 4.)

Applicants strongly disagree with the Examiner's position and traverse the rejection.

First, it is noted that the sequence the Examiner used to produce the alignment that was sent with the Office Action is not the reticulocalbin sequence that was published on page 701 of the Ozawa et al. article. A careful visual comparison of the sequences reveals that the sequence used to produce the alignment labeled "RESULT 2" on page 2 of the document generated on Tue Feb 25 16:40:19 2003 is 315 AA in length and begins with "MDLRQFLMC..." The reticulocalbin sequence published at page 701 of the Ozawa et al. article is 325 AA in length and begins with "MARGGRLGLALG..." Clearly, these are not the same sequences. Of particular note is that the 315 AA sequence in the alignment was submitted in ***October 1997*** and created in the TrEMBLrel. Database on January 1, 1998. The priority date of the instant application is ***August 8, 1997***. Therefore, this sequence is not prior art to SEQ ID NO:3.

The attached CLUSTALW alignment (Attachment 2) of SEQ ID NO:3 (1601793CD1) with the reticulocalbin sequence published in Ozawa et al. (g220582) indicates that there is a 60% sequence identity (192/315 amino acids) between the two sequences--and the sequence identity is only that high because the CLUSTALW program inserted five gaps in SEQ ID NO:3 to effect the alignment. Additionally, Applicants submit that the rejection cannot withstand further scrutiny of the law under 35 U.S.C. § 102.

The MPEP is clear with regard to the requirements for making a rejection under any subsection of 35 U.S.C. § 102:

> for anticipation under 35 U.S.C. 102, ***the reference must teach every aspect of the claimed invention either explicitly or impliedly***. Any feature not directly taught must be inherently present. (*MPEP 706.02* at page 700-21, Rev. 1, Feb. 2003) [Emphasis added.]

The polypeptide sequence taught by Ozawa et al. does not ***teach every aspect of the claimed invention either explicitly or impliedly***. The Examiner has alleged that the polypeptide sequence taught by Ozawa et al. (reticulocalbin) is 89.1% identical to SEQ ID NO:3 (RCNδ). (Office Action at page 4.) As noted above, the reticulocalbin taught by Ozawa et al. is only 60% identical to SEQ ID NO:3. It is, therefore, possible to make an antibody to SEQ ID NO:3 that does not bind reticulocalbin. Such an antibody is recited in claim 10 as "An isolated antibody ***which specifically binds*** to a polypeptide comprising the amino acid sequence of SEQ ID NO:3." By **"specifically binding"** to SEQ ID NO:3, the claimed antibody ***must*** bind to a polypeptide consisting of SEQ ID NO:3. Accordingly, so long as there are differences, even just one amino acid residue, between the amino acid sequence recited in claim 10 and that disclosed in Ozawa et al., an antibody can be produced that can specifically bind to the polypeptide recited in claim 10 and not that of reticulocalbin.

Evidence in support of this premise may be found in Abaza et al., J. Protein Chem. (1992) 11:433-444 (Attachment 1). As taught by Abaza et al., a single amino acid substitution outside the antigenic site on a protein effects antibody binding. This provides scientific support of Applicants' assertion that so long as there are differences, even just one amino acid residue, between the amino acid sequence of claim 10 and those of the prior art, an antibody can be produced that can specifically bind to the polypeptide recited in claim 10 and not those of the prior art. Accordingly, given the

extensive amino acid differences between SEQ ID NO:3 and reticulocalbin (at least 40%), one of skill in the art could produce an antibody which binds to the polypeptide recited in claim 10 alone and without cross-reactivity to other polypeptides even those which have extensive sequence identity to SEQ ID NO:3, which reticulocalbin does not have.

Once claim 10 (and therefore claims 30, 36 and 39) has been correctly characterized and considered in its proper context, the ancillary issues regarding antibodies in composition (claims 31, 37 and 40), having a label (claim 33), or being produced by either a Fab expression library or an immunoglobulin expression library (claims 41 and 42) become moot. For at least the above reasons, Applicants respectfully request that this rejection be withdrawn.

CONCLUSION

In light of the above amendments and remarks, Applicants submit that the present application is fully in condition for allowance, and request that the Examiner withdraw the outstanding objections/rejections. Early notice to that effect is earnestly solicited.

If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, Applicants invite the Examiner to contact the undersigned at the number listed below.

Applicants believe that no fee is due with this communication. However, if the USPTO determines that a fee is due, the Commissioner is hereby authorized to charge Deposit Account No. **09-0108.**

Respectfully submitted,

INCYTE CORPORATION

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Attachments:

Attachment 1: Abaza et al., J. Protein Chem. (1992) 11:433-444
Attachment 2: CLUSTALW alignment of g220581 and SEQ ID NO:3, including NCBI documents for g220581 (3 pages)